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10/715,017	11/17/2003	Arun Majumdar	028726-022	3299

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EXAMINER

LUM, LEON YUN BON

ART UNIT	PAPER NUMBER
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1641

DATE MAILED: 04/04/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

## Office Action Summary

Application No.

10/715,017

Applicant(s)

MAJUMDAR ET AL.

Examiner

Leon Y. Lum

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

### Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

### Status

- 1) ☒ Responsive to communication(s) filed on 13 January 2006.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

### Disposition of Claims

- 4) ☒ Claim(s) 1-82 is/are pending in the application.
- 4a) Of the above claim(s) 1-63 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 64-82 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

### Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
- ☐ Certified copies of the priority documents have been received.
  - ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  - ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

### Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08)  
Paper No(s)/Mail Date \_\_\_\_\_.
- 4) ☐ Interview Summary (PTO-413)  
Paper No(s)/Mail Date. \_\_\_\_\_.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: \_\_\_\_\_.

**DETAILED ACTION**

1. The amendment filed January 13, 2006 is acknowledged and has been entered.

***Election/Restrictions***

2. Applicant's election without traverse of claims 64-82 in the reply filed on January 13, 2006 is acknowledged.

***Priority***

3. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. [1] as follows: Claim 69 as amended recites a "strengthening ridge" on the claimed reflective paddle. However, provisional application 60/426,851 to which Applicants claim benefit do not provide support for the "strengthening ridge" in the specification, drawings, or claims. Claim 69 is therefore not given the benefit of the filing date of provisional application 60/426,851, and the effective date against the instant claim is the filing date of the instant application, November 17, 2003.

***Claim Rejections - 35 USC § 103***

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

5. The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

6. This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

7. Claims 64-68, 70-73, 77-80, and 82 are rejected under 35 U.S.C. 103(a) as being obvious over Fritz et al. (Science, 2000) in view of Ellerbrock et al (US 6,204,920 B1).

Fritz et al reference teaches eight cantilevers in a microfabricated silicon cantilever array (i.e. array of microsensors; membranes linear array; two-dimensional array), each cantilever functionalized on one side with a different oligonucleotide base sequence (i.e. functionalized), wherein hybridization of the base sequences with complementary oligonucleotide causes functionalized cantilever to bend (i.e. deflect when exposed to target molecules). See Figures 1-2 and captions. In addition, Fritz et al teach that the bending of each cantilever is measured using an optical beam deflection technique that detects reflected light (i.e. an optical beam source; an optical detector), wherein a linear VCSEL array provides a surface-emitting laser (i.e. collimated beam of laser light) to each cantilever (i.e. configured to simultaneously direct an optical beam onto each of the microsensors). See page 316, middle column, 2<sup>nd</sup> paragraph, lines 11-13; and page 318, right column, reference 14. Furthermore, Fritz et al teach that absolute deflections and simultaneous differential signals were recorded during hybridization (i.e. detector array simultaneously detect the position of each of the microsensors; detection in real time; detecting movement of beams of light reflected by each of the microsensors). See page 316, right column, 1<sup>st</sup> paragraph, lines 20-27.

However, Fritz et al fail to teach that the optical beam source is a *single* optical beam source configured to simultaneously direct an optical beam onto each of the microsensors in the array of microsensors.

Ellerbrock et al reference teaches a single light source that is multiplexed, in order to address multiple sensors while reducing cost of the system with just one light source. See column 2, lines 19-31; column 4, lines 45-67; and Figure 2. In addition, Ellerbrock et al teach that the light source can emit laser light. See column 5, lines 38-42.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the VCSEL array of Fritz et al with a single light source that is multiplexed, as taught by Ellerbrock et al, in order to address multiple sensors while reducing cost of the system with just one light source. The advantage of producing an optical system without requiring multiple light sources provides the motivation to combine the single light source of Ellerbrock et al with the apparatus of Fritz et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the single light source of Ellerbrock et al in the apparatus of Fritz et al, since Fritz et al teach laser light sources, and the single light source of Ellerbrock et al can also be a laser light source.

With regards to claims 67-68, Fritz et al teach that the base sequences are immobilized on the gold-covered side (i.e. reflective paddle; stiffened portion) of the cantilevers. See page 316, middle column, 2<sup>nd</sup> paragraph, line 14 to right column, 1<sup>st</sup> paragraph, line 2.

With regards to claim 77, Fritz et al teach that one cantilever is functionalized with a 12-mer oligonucleotide and another with a 16-mer oligonucleotide (i.e.

functionalized to detect different target molecules). See page 316, right column, 1<sup>st</sup> paragraph, lines 2-6.

With regards to claims 78 and 80, Fritz et al teach that hybridization experiments were performed in a liquid cell (i.e. at least one of the microsensors is positioned to be submerged in a fluid cell), wherein buffer solution is manually exchanged by a micropipette (i.e. flow of fluid sample can be stopped in the fluid cell). See page 316, middle column, 2<sup>nd</sup> paragraph, lines 8-11; and page 318, reference 13.

With regards to claim 79, since Fritz et al teach that hybridization is performed in a fluid cell and that optical detection is performed in real time, as stated above, it is necessarily required that the fluid cell be transparent to the optical beam in order to perform the hybridization assay and detection

8. Claim 69 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fritz et al. (Science, 2000) in view of Ellerbrock et al (US 6,204,920 B1) as applied to claims 64-65 and 67 above, and further in view of Glezer et al (US 2004/0189311 A1).

Fritz et al and Ellerbrock et al references have been disclosed above, but fail to teach that the reflective paddle portion includes a strengthening ridge.

Glezer et al reference teaches a ledge surrounding a coated binding region, in order to provide a barrier that confines deposited fluid to the binding region. See page 17, section 0155. The Glezer et al reference is an intervening reference. See **Priority** section above.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the cantilever sensors of Fritz et al and Ellerbrock et al with a ledge surrounding the binding region, as taught by Glezer et al, in order to provide a barrier that confines deposited fluid to the binding region. The ledge prevents fluids and any analytes therein from moving away from the binding region, which is motivation to combine the ledge of Glezer et al with the cantilever sensors of Fritz et al and Ellerbrock et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including the ledge of Glezer et al in the apparatus of Fritz et al and Ellerbrock et al, since Fritz et al and Ellerbrock et al teach binding regions on a surface, and the ledge of Glezer et al is provided for the specific purpose of surrounding a binding region on a surface.

9. Claim 74 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fritz et al. (Science, 2000) in view of Ellerbrock et al (US 6,204,920 B1) as applied to claim 64 above, and further in view of Park et al (US 5,448,399).

Fritz et al and Ellerbrock et al references have been disclosed above, but fail to teach that the optical detector array is a CCD array.

Park et al reference teaches a CCD camera that captures reflected light from a sample on a cantilever, in order to output an image of a probe or sample to a video display. See column 25, lines 31-40.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the cantilever array of Fritz et al and Ellerbrock et al with a CCD



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camera that captures reflected light from a sample on a cantilever, as taught by Park et al, because the CCD camera provides an image of sample capture on the cantilever, which is more easily visualized than the graphical representations of Fritz et al and Ellerbrock et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a CCD camera, as taught by Park et al, in the apparatus of Fritz et al and Ellerbrock et al, since Fritz et al and Ellerbrock et al teach optical means of detecting cantilever deflection, and the CCD camera of Park et al is one type of optical means to detect deflection of cantilevers.

10. Claim 75 is rejected under 35 U.S.C. 103(a) as being unpatentable over Fritz et al. (Science, 2000) in view of Ellerbrock et al (US 6,204,920 B1) as applied to claim 64 above, and further in view of Quate et al (US 6,203,983).

Fritz et al and Ellerbrock et al references have been disclosed above, but fail to teach that the optical detector array is a CMOS array.

Quate et al reference teaches a CMOS microelectric processing system, in order to easily integrate with silicon-based micromechanical devices such as cantilevers and to produce seamless sensors at low cost and integrate them directly into computers. See column 2, lines 11-23.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the cantilever array of Fritz et al and Ellerbrock et al with a CMOS microelectric processing system, as taught by Quate et al, because the CMOS detectors are low cost, can be easily integrated into computers, and can be utilized with

silicon-based cantilevers. The ease of use and economic incentive provide the motivation to combine the CMOS detectors of Quate et al with the apparatus of Fritz et al and Ellerbrock et al. In addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a CMOS system, as taught by Quate et al, in the apparatus of Fritz et al and Ellerbrock et al, since Fritz et al and Ellerbrock et al teach silicon-based cantilevers, and the CMOS system of Quate et al can be integrated with silicon-based cantilevers.

11. Claims 76 and 81 are rejected under 35 U.S.C. 103(a) as being unpatentable over Fritz et al. (Science, 2000) in view of Ellerbrock et al (US 6,204,920 B1) as applied to claim 64 above, and further in view of Lee et al (US 5,807,758).

Fritz et al and Ellerbrock et al references have been disclosed above, but fail to teach that at least one microsensor is not functionalized to deflect when exposed to the target molecules.

Lee et al reference teaches a reference cantilever 82 (i.e. microsensor not functionalized) in proximity to a modified cantilever 12, in order to eliminate sources of noise, including non-specific binding. See column 8, lines 44-64; and Figure 8.

It would have been obvious to one of ordinary skill in the art at the time of the invention to modify the cantilever array of Fritz et al and Ellerbrock et al by placing a reference cantilever in proximity to a modified cantilever, as taught by Lee et al, in order to eliminate sources of noise, including non-specific binding, which allows clearer detection of sample binding on the cantilever array of Fritz et al and Ellerbrock et al. In

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addition, one of ordinary skill in the art at the time of the invention would have had reasonable expectation of success in including a reference cantilever, as taught by Lee et al, in the apparatus of Fritz et al and Ellerbrock et al, since Fritz et al and Ellerbrock et al teach an array of cantilevers, and the reference cantilever of Lee et al is capable of being placed in an array of cantilevers.

With regards to claim 81, Lee et al teach that the cantilever can be detected by an interferometer. See column 8, lines 31-40.

### ***Response to Arguments***

12. On pages 15-16 of the response filed January 13, 2006, Applicants traverse the rejections of the previous Office Action by submitting two specific arguments:

- (1) Fritz et al reference does not teach the claimed "single optical beam source" as recited in claim 64.
- (2) Fritz et al reference does not teach the claimed "optical detector array" since the lasers are taught to share the same linear position-sensitive detector.

With respect to Applicants' first argument above, it has been fully considered but is moot in view of the new ground(s) of rejection as necessitated by the claim amendment.

With respect to Applicants' second argument above, Fritz et al do in fact teach a detector array. In the response on page 15, Applicants point to endnote 14 on page

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318 of Fritz et al reference, which teaches "Detection of the reflected light by a single linear position-sensitive detector". Applicants interpreted this phrase to mean that all cantilevers are detected by the same detector. However, it is clear from the disclosure in the main body of the reference that each cantilever has a dedicated detector. On page 317, Figure 3 shows a hybridization experiment in which the sensor pair shown in Figure 2 is simultaneously exposed to three different solutions in sequence, labeled as sequences I-III. Figure 3A specifically shows the deflection of both sensors during real-time measurement of each sequence I-III, which indicates that simultaneous measurements of two reflected light signals are obtained. Since endnote 14 on page 318 indicates that each reflected light is detected by one detector, it is necessarily required that two detectors are present during the hybridization assay to detect reflected light from each of the cantilevers. Applicants' argument that Fritz et al do not teach a detector array is therefore not found convincing since Fritz et al clearly teaches an array of detectors.

### ***Conclusion***

13. No claims are allowed.

14. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP

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§ 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leon Y. Lum whose telephone number is (571) 272-2878. The examiner can normally be reached on weekdays from 8:00am-5:00pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Leon Y. Lum  
Patent Examiner  
Art Unit 1641



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